Aorta

Introduction to the Aorta

The aorta is the largest artery in the body. Like all arteries, it has an adventitia, media, and intima. The intima is the endothelium and its basement membrane. The adventitia is connective tissue with vasa vasorum. The media contains vascular smooth muscle cells (VSMC), elastin, and collagen. The aorta is the large elastic artery that distends during systole and recoils—sustaining the perfusion pressure—during diastole. It is also connected to the left ventricle. The most applied force, the most trauma, and therefore the most wear and tear, occurs to the aorta. When you add on additional insults—atherosclerosis, cystic medial degeneration, hyaline arteriolosclerosis (terms you aren't expected to know yet)—the aorta can break.

The **ascending aorta** is the region from the aortic root up to the brachiocephalic artery; it supplies the coronary ostia during diastole. The **transverse arch** contains the brachiocephalic, left carotid, and left subclavian arteries, supplying the entire vascular supply of the head and arms. It continues until the remnant of the ductus arteriosus, the ligamentum arteriosus. The **descending thoracic aorta** runs from the ligamentum arteriosum to the diaphragm, its branches supplying blood to ribs and chest structures. The **abdominal aorta** runs from the diaphragm, supplying all of the abdominal organs, until it splits into the iliac arteries.

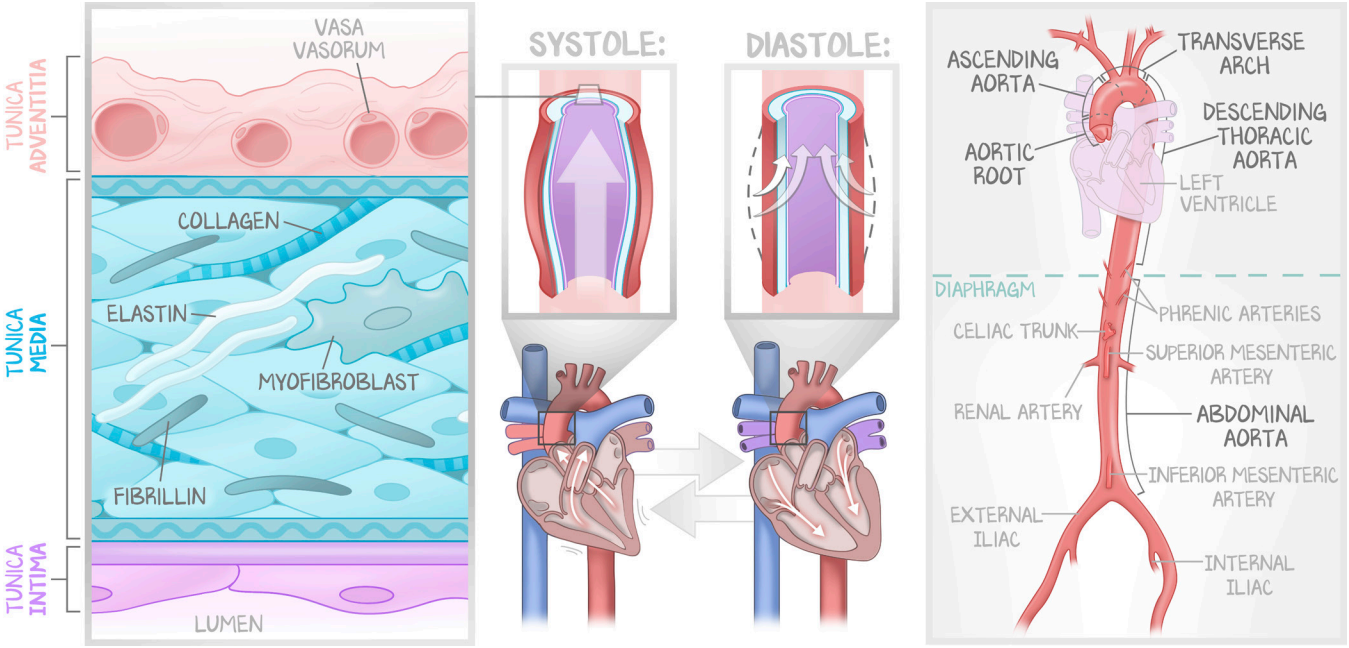

Figure 3.1: The Aorta Model
The aorta is an artery; it distends and recoils in response to ventricular contraction (systole) and relaxation (diastole). It has a tunica adventitia, tunica media, and tunica intima. What we want to do here is expand on the aorta using the three-tunicae model. The pathologies in this lesson have to do with a compromised tunica media—collagen, elastin, fibrillin, myofibroblasts/VSMC. In this lesson, the pathogenesis of aortic disease is either a pathology from outside the tunica media—within the tunica adventitia or tunica intima—or from inside the tunica media, such as genetic defects. Aortic disease is so important because the aorta is the first blood vessel—the thoracic aorta providing all of the blood supply to the head and upper extremities (arteries arising from the transverse arch) and the abdominal aorta supplying the viscera in the abdomen and pelvis, as well as branching to form the vessels of the lower extremities.

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The aorta is a stretchy tube. It distends then recoils. It both accepts (and stores) the perfusion pressure from the ventricle and opposes that pressure. Without elastin, the aorta would distend but fail to recoil. That is called an **aneurysm**. Without collagen, the aorta could rip apart. That is called a different name based on its severity—aortic **hematoma**, aortic **dissection**, and aortic **transection**, listed in order of increasing danger. These things can happen in the **thoracic** or **abdominal** aorta. It is the same vessel, but the location matters because of the potential consequences. Finally, there are congenital defects that involve the aorta, specifically **aortic coarctation**.

And that is what this lesson is about. You warm up with some histology you already know superimposed on the general anatomy of the aorta. Then we explore, in general, how the aorta may become irreparably damaged, and close by reviewing the diagnosis for each of the disease states stated in the last paragraph.

Pathogenesis of Aortic Aneurysmal Diseases

The aorta is a stretchy tube (repeated for emphasis). Being a blood vessel, there aren't many things that can go wrong because it is little more than a stretchy tube. And all of the pathologies in this lesson have to do with the tunica media. But the aorta is an artery, and other pathologies can occur. The pathology of the endothelium/tunica intima we will see in atherosclerosis in the Coronary Artery Disease island and the Pulmonary Circulation island of the Pulmonary module.

How do we get a weakened tunica media? There are three possible mechanisms: hyaline arteriosclerosis of the vasa vasorum, atherosclerosis of the aorta itself, and genetic defects in the tunica media. All three lead to **cystic medial degeneration**, characterized by the histological changes of scarring (fibrosis results in a nonelastic extracellular matrix), loss of VSMC, and production of an amorphous ground substance. The tunica media degenerates, atrophies, gets weaker. Let's first explore how it happens, then turn our attention to its consequences.

Hyaline arteriolosclerosis. The vasa vasorum are the small arteries in the adventitia of the aorta that perfuse the aorta—they are the blood vessels of blood vessels. Like all small vessels in the body, these small arteries respond to certain stresses by depositing extracellular proteins. This concept, the deposition of extracellular protein, is new to you. We will go into much detail later in the lessons on hypertension and even more in the diabetes lessons in the Endocrine module. The deposition of extracellular protein is called **hyaline arteriolosclerosis**. Notice that it is hyaline arteriolo-sclerosis. Sclerosis means hardening but is also the term used for "compromised lumen of a blood vessel." Hyaline means glass-like and is used to describe "pink stuff without nuclei that isn't collagenous fibrosis." We didn't make these terms up or decide how they would be used. Bottom line, the leaky endothelium of arterioles and small arteries results in the deposition of protein in the tunica intima. This is a concentric deposition—all the way around the arteriole equally. And it isn't just one blood vessel—it happens to all of them, everywhere. With a narrowed lumen, the vasa vasorum delivers oxygen to the outer layers of the tunica media less efficiently. Without oxygen, over time, they die. **Hypertension** and **diabetes** produce the histological finding of hyaline arteriolosclerosis, and the narrowing of the lumen leads to cystic medial degeneration, the weakening of the tunica media. These are considered the microvascular complications of hypertension and diabetes. For the Cardiac module, because you haven't yet learned about diabetes, we want you to associate **career hypertension** (high blood pressure for a very long time) with **hyaline arteriolosclerosis**.

Atherosclerosis. Chronic hypertension and diabetes are also major risk factors for the development of atherosclerosis. Atherosclerosis is the formation of a **plaque**, discussed in CAD (Coronary Artery Disease) #1: *Pathophysiology of Atherosclerosis.* A necrotic lipid core forms between the tunica intima and its basement membrane. Myofibroblasts proliferate from the tunica media to cover the lipid core and shield it from the bloodstream. This keeps the plaque stable but adds a thicker diffusion barrier for oxygen. The vasa vasorum is required to perfuse the outer tunica media because it is so large. The inner tunica media

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relies on oxygen diffusion from the lumen. Just as hyaline arteriolosclerosis in the vasa vasorum increases the diffusion barrier for oxygen, an atherosclerotic plaque increases the barrier that oxygen from the lumen must diffuse through. Either way, you get a weakened tunica media and cystic medial degeneration. Atherosclerosis risk factors include hypertension and diabetes. Like we did in the last paragraph, we want you to associate **career smoker** (many years of smoking many cigarettes) with atherosclerosis.

The reason we do this is so you can keep things siloed. By the time you get to the CAD island, you will have already figured out that this is an oversimplification. We do it because we expect you to know very little about organ systems now. Career hypertension, arteriolosclerosis; career smoker, atherosclerosis.

Genetics. The first two were complications of chronic disease. Both atherosclerosis and hyaline arteriolosclerosis can occur in any blood vessel, but we are focused on their impact on the aorta specifically. There are genetic diseases that start with an impaired and weakened tunica media. Elastin is laid down and organized by fibrillin and linked together by collagen (don't get into the specifics; just know that). A genetic defect in **fibrillin** (as in Marfan's syndrome, caused by an autosomal-dominant mutation of *FBN1* on Chr 15) will result in a tunica media riddled with faulty elastin, impairing elastic recoil. A genetic defect in **collagen** (as in Ehlers-Danlos syndrome, caused by genes that impact the synthesis of collagen III) will result in a tunica media that is less able to resist distending forces and a weaker foundation for elastin, also impairing elastic recoil.

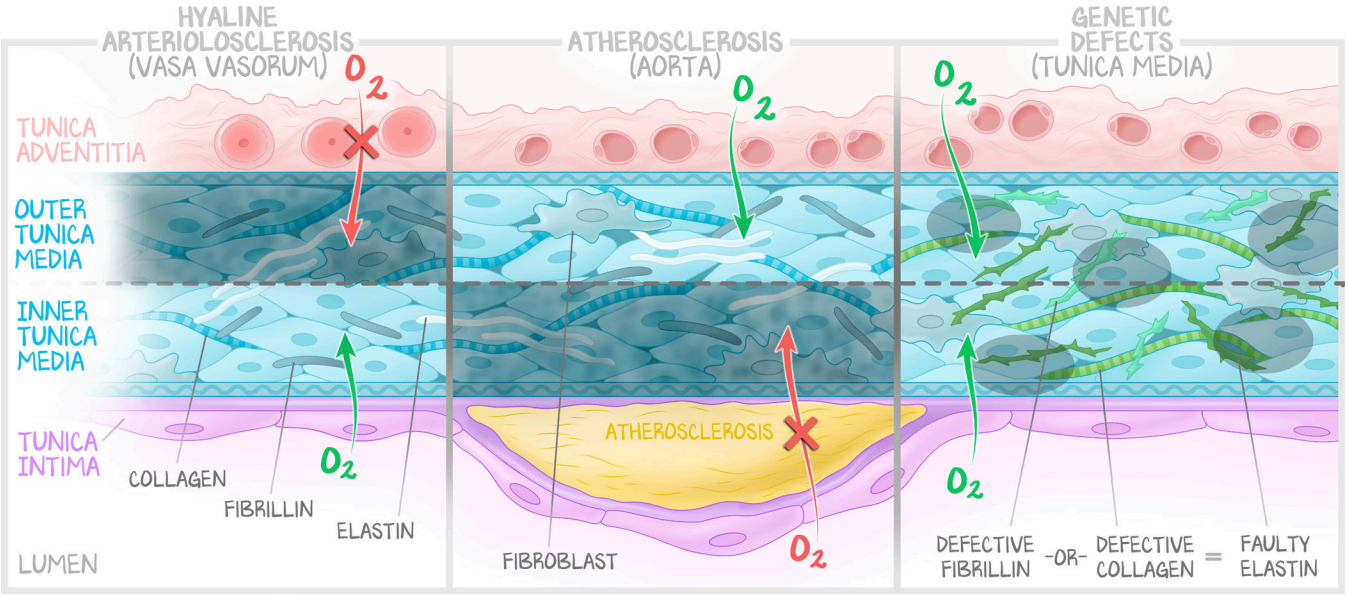

Figure 3.2: Pathogenesis of Aneurysmal Disease
Hyaline arteriolosclerosis secondary to chronic hypertension or diabetes prevents perfusion of the outer tunica media, resulting in cystic medial degeneration of the outer media (represented by the darkened region of the tunica media). Atherosclerosis prevents luminal diffusion of oxygen to the inner tunica media, resulting in cystic medial degeneration of the inner media (represented by the darkened region of the tunica media). This is a model—outer vs. inner isn't exactly halfway—and a guide to aid in the comprehension of the concept. Finally, genetic defects in elastin, collagen, or fibrillin inherently compromise the elastin layer despite normal perfusion of the tunica media—it is perfused, but its elastin fibers and network fail. Because the pathology is inherent to the cells of the tunica media, cystic medial degeneration occurs sporadically, represented by the darkened ovals.

Special circumstances mirror the three main defects. **Tertiary syphilis** results in arteritis, inflammation of the small vessels. The vasa vasorum are small vessels. Inflammation of the vessel walls leads to reduced blood flow, mirroring hyaline arteriolosclerosis. This histology will show vasculitis—inflammatory cells in the vessel wall—rather than a thickened wall as with hyaline arteriolosclerosis. But the pathogenesis

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of poor tissue perfusion to cystic medial degeneration leads to the same outcome. Tertiary syphilis is associated with thoracic aortic aneurysm. **Scurvy**, vitamin C deficiency, causes defective collagen synthesis that mirrors that in Marfan's and Ehlers-Danlos.

Spectrum of Aneurysmal Diseases

This section is used to build your vocabulary before moving forward. These disease states have overlapping names and overlapping criteria, so you may get tripped up the first time you encounter them.

There are true aneurysms, hematomas and dissections, false aneurysms, and transections.

A **true aneurysm** is a defect of elastic recoil. What makes an aneurysm "true" is if it involves all three layers. That is to say, the tunica intima, media, and adventitia are in normal relation to one another, still attached together, but bulging outward. This is usually a consequence of impaired elastin—the artery distends but fails to recoil. There are different types of true aneurysms, and they can occur in any blood vessel. You will encounter berry aneurysms or saccular aneurysms as the cause of brain bleeds. Here, in cardiac, "true aneurysm" is of one kind—that caused by cystic medial degeneration. Just as the remaining diseases are.

A false aneurysm isn't the opposite of a true aneurysm. It is actually one step before complete transection. So, we continue this discussion in order of increasing severity and acuity.

An aortic **hematoma** is blood in a false lumen that isn't worsening. An aortic **dissection** is blood in a false lumen that is continuing to expand, dissecting the tunica media as it does. This is caused by a tear through the tunica intima and into (but not through) the tunica media.

A **false aneurysm** is when there is a tear through the tunica intima and tunica media. The false lumen is formed between the tunica adventitia and the tunica media. This is really bad. The adventitia isn't meant to sustain the pulsatile force of the ventricle. This is one step before rupture or transection.

A **transection** occurs when a false aneurysm's adventitia fails, and each heartbeat spills blood into the mediastinum. The ligamentum arteriosum is at the aortic arch. In severe deceleration injuries (80-mph motor vehicle collision against a concrete bridge abutment), the car stops, you stop, but the viscera continue forward. The ligamentum arteriosum does not act like a seatbelt, but rather a razor wire, shearing the aorta. This is almost always fatal on the scene.

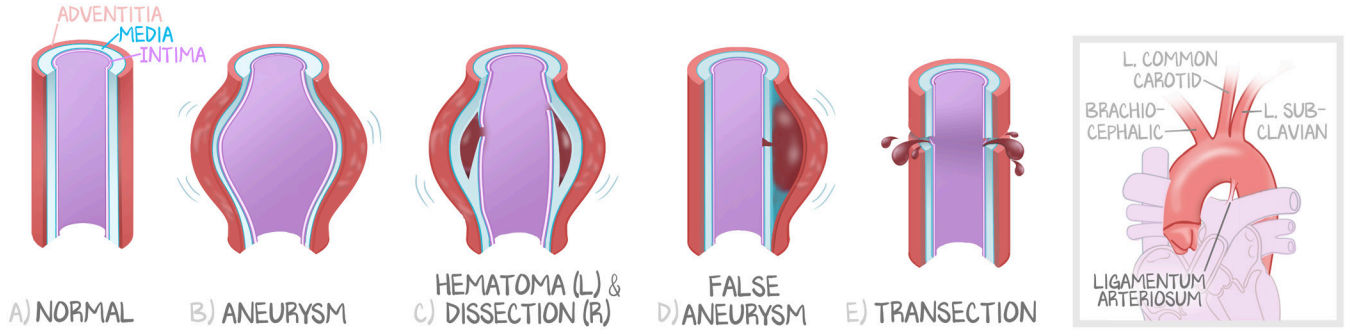

Figure 3.3: Spectrum of Aneurysmal Diseases
This illustration visualizes the previous paragraph. All vessels can have a true aneurysm, hematoma and dissection, false aneurysm, or transection. The aorta is such an important artery (giving rise to all arteries), so it gets special attention. Introduce, visualize, and familiarize yourself with the concepts as they pertain to the aorta, but know that these extend beyond "pathologies of the aorta."

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Abdominal Aortic Aneurysm (AAA)

An abdominal aortic aneurysm (AAA, pronounced "*triple A*") is an aneurysm of the abdominal aorta—from the diaphragm to its bifurcation into the common iliac arteries just above the pelvis. Most AAAs occur **below the renal arteries** and **before the bifurcation into the common iliac arteries**. Being near the renal artery, the progression of the aneurysm can involve the renal structures, leading to **renal failure**. AAA is a true aneurysm—all three tunicae in the outpouching. The abdominal aorta is the farthest from the source of transluminal stress—the most distal from the left ventricle. For that reason, dissections and hematomas generally don't occur here. The main pathogenesis of AAA is **atherosclerosis**, the formation of a plaque that impairs luminal diffusion of oxygen.

The population with the highest incidence is **male smokers**. Being male and being a career smoker both increase the risk of atherosclerosis and the AAA that atherosclerosis causes. There are two AAA presentations we want you to associate with the illness script at this point in your training: asymptomatic and rupture. **Asymptomatic** AAA will be diagnosed with **screening ultrasound** at age **65**. This screening is performed for all males with a smoking history. The other presentation will be in an **old man** who **used to smoke** and now has **back pain** and a **pulsatile abdominal mass**. The pain is referred pain from the aorta, which has become so distended it is about to rupture.

Diagnosing a AAA is best done with an ultrasound—noninvasive, cheap, and very effective. The diagnosis may also be made using CT angiography or MR angiography. These are effective at showing not only the lumen of the aorta but also the surrounding soft tissue. Angiography—injecting dye into the aorta through a wire—is performed only for (and during) therapeutic intervention. It was formerly a big deal to remember NOT to choose angiography to diagnose AAA because the atherosclerosis or mural thrombus can "fill in" the aneurysm, and with angiography, there is no visualization of the soft tissue around it. With access to CT and MRI, where a contrast dye is injected into a peripheral vein (no wire), and with three-dimensional reconstructions of all the vessels and organs around it, the consideration of angiography with a wire is better left for the vascular surgeon who is going to treat the AAA.

Treatment is surgical. Surgery is performed when an aneurysm is big (greater than 5.5 cm) or growing quickly (greater than 0.5 cm/year). Once diagnosed, annual ultrasounds track the changes.

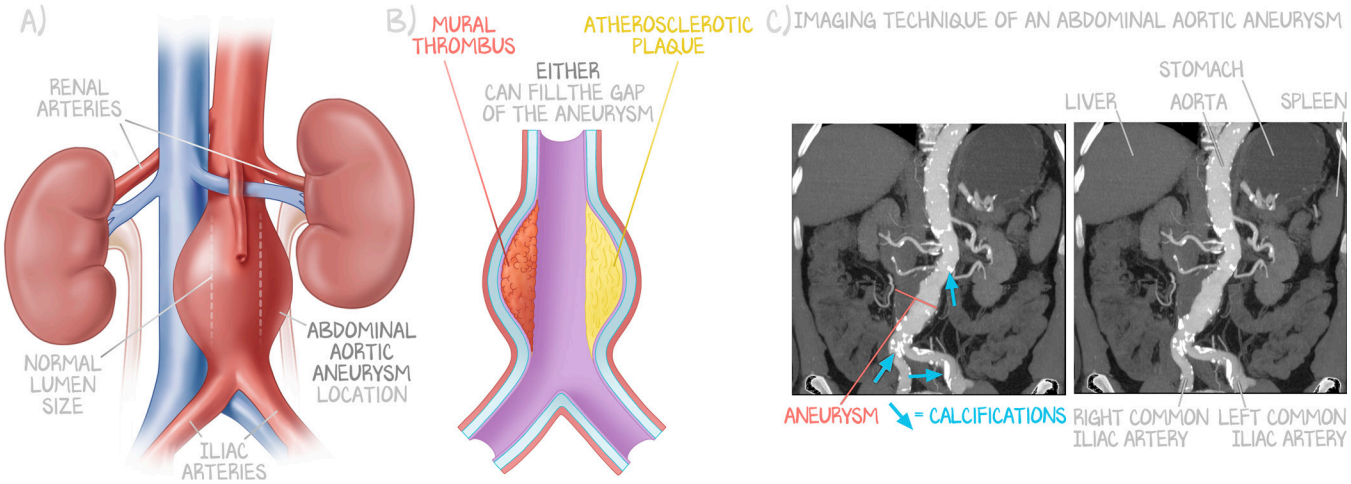

Figure 3.4: Abdominal Aortic Aneurysm
(a) The usual location of an AAA, distal to the renal arteries. The outpouching tells you there is pathology, but you can't be certain what's underneath. (b) Atherosclerosis caused the aneurysm, and a mural thrombus formed in the wall of the aneurysm. This is purposefully illustrated with a "normal lumen" (purple) to reinforce why angiogram alone would be insufficient to diagnose AAA. (c) CT with intravenous contrast showing the abdominal aorta and the major branches. All of the bright white spots are calcifications, indicative of atherosclerosis. The light grey is the lumen, which appears normal at the spot marked aneurysm. Because CT scans do see soft tissue, the aneurysm, which does not have blood in it (it would be light grey if it did), can still be visualized.

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There are three major consequences of a AAA. A large AAA can rupture, which is fatal. If a AAA grows up (acting more like a dissection than an aneurysm) and involves the renal artery, it can lead to **renal failure**. Either because of the atherosclerosis that caused it or the formation of a blood clot in the wall of the aneurysm (a mural thrombus), there can be embolism of the clot down to the lower extremities, causing **acute limb ischemia**.

Aortic Dissection

Aortic dissection is an **expanding hematoma**. Hematoma means the pooling of blood. It is called dissection because the hematoma is forming **within the tunica media**. There is a tear through the tunica intima (easy, as it's just one cell thick) and **partially** through the tunica media. The hematoma is contained by both the entirety of the tunica adventitia and the untorn outer tunica media. With each heartbeat, blood goes down the aorta as it should, but it also pushes more blood through the defect in the aorta wall, feeding more blood into the **false lumen**. With more blood in the false lumen, the pressure exerted causes the dissection to get wider at the site of the wall defect but also pushes blood along the length of the aorta, extending the dissection, expanding the hematoma.

This is a result of high pressure. There must be both a **career hypertensive** (who has developed hyaline arteriolosclerosis) and a **hypertensive crisis** (sudden very high blood pressure). These are both OME terminology, not formal diagnoses. We use them to help you remember that what rips the wall of the aorta is very high blood pressure all of a sudden (hypertensive emergency) in a person with persistent, chronic hypertension (cystic medial degeneration). The "classic triad" (usually not all three are present at once, but finding two of the three has a high likelihood ratio for dissection) is **tearing chest pain that radiates to the back**, the finding of **unequal blood pressures in upper extremities**, and a **widened mediastinum** on chest X-ray (though there is no formal cutoff for what "widened" means). The diagnosis is confirmed with a **CT angiogram**, which will reveal the false lumen. Other ways to assess for dissection include transesophageal echocardiogram and MRI. See these words, but note that they are not in bold. We will discuss when to pick each, but not until Clinical Sciences.

Treatment depends on where the dissection is. An **ascending dissection** (Stanford class A, DeBakey class II) involves the aortic root to the brachiocephalic branch—before the major vessels leading to the brain and upper extremity. **Emergent surgery** is required as the dissection can advance to compromise the circulation to the brain, causing a stroke. A **descending dissection** (Stanford class B, DeBakey class III) involves the aorta after the left subclavian artery down. This is treated with intravenous **esmolol** (a β-blocker that slows the heart rate and reduces the force of contraction). A combined dissection (Stanford class A, DeBakey class I) is both.

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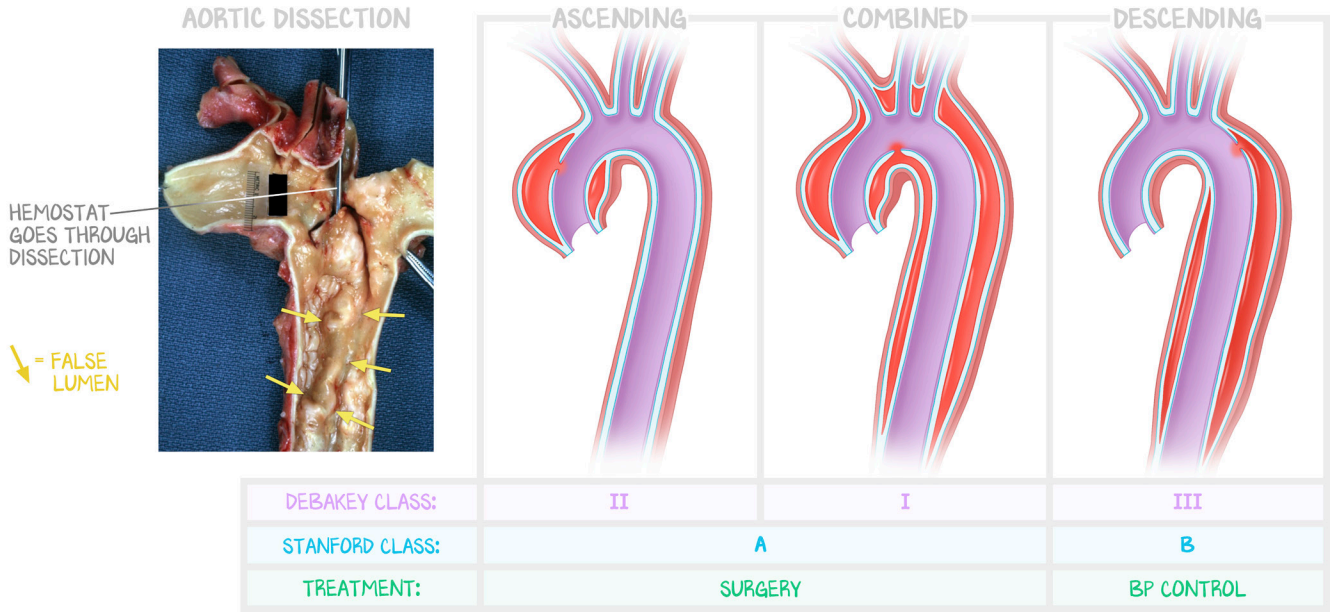

Figure 3.5: Aortic Dissection

Complications of the dissection depend on where it is. Surgery is required for ascending dissections because if the dissection moves retrograde, it can result in dilation of the aortic root. That dilation can, in turn, cause aortic insufficiency, pericardial hemorrhage, or **pericardial tamponade** (death). If an ascending dissection moves anterograde, any of the blood vessels to the upper extremity and brain can be compromised, resulting in infarction of the arms or stroke. Descending dissection can continue into the renal arteries, resulting in renal failure.

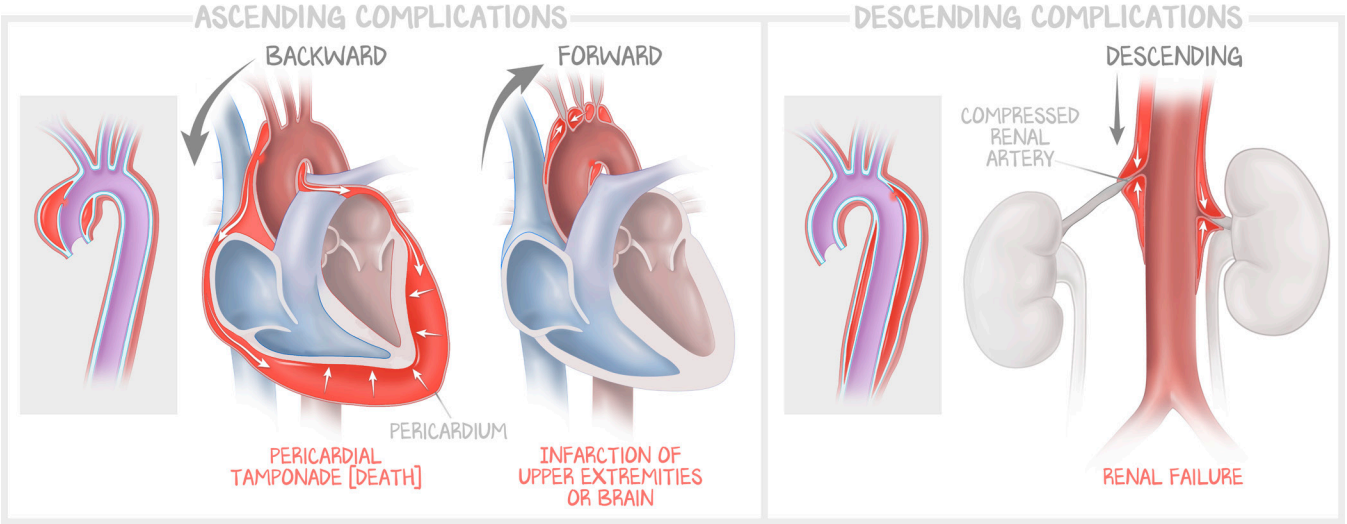

Figure 3.6: Complications of Dissection

Thoracic Aortic Aneurysm

A thoracic aortic aneurysm is the AAA of the chest. In life, the most common cause of aneurysm is either career hypertension leading to hyaline arteriolosclerosis or smoking causing atherosclerosis. On licensure exams, AAA is seen in old men who smoke, and thoracic dissection is seen in career hypertensives, with thoracic aneurism usually as the odd one left out. It presents very differently from the others, with symptoms secondary to compression. It is an aneurysm, can have mural thrombus, and can embolize, causing acute limb ischemia. The illness script you are looking for when taking the test is the person with **tertiary syphilis**. The pathogenesis of syphilitic aortitis (aorta inflammation secondary to syphilis) is nearly identical (both in physiology and what you see on histology) to hyaline arteriolosclerosis causing cystic medial degeneration. The only difference is how that histological appearance came about.

You should look for a person with **low socioeconomic status**, **unsafe sex practices**, and a history of multiple **sexually transmitted infections**. There may be other signs of neurosyphilis, and although the person did have a chancre and a secondary reaction, the recall of that syphilitic reaction will be denied. The vignette needs to keep it hard enough so that the answer is not immediately obvious but arm you with enough information that you can say, "this case isn't atherosclerosis or hypertension."

This is a true aneurysm, and the outpouching of the thoracic aorta can impact the other structures in the thorax. **Compression of mediastinal structures** may result in **hoarseness**, **dysphagia**, or **cough**. This aneurysm can progress like a dissection, anterograde or retrograde, even though the tunica intima is intact. This progression is of the true aneurysm; so, unlike the dissection, which is a bleed, the outcome of this progression is less severe. Thoracic aneurysms cannot bleed into the pericardial space, so they cannot cause tamponade, nor can they compress the arteries of the head and arms. But the aneurysm can progress to the aortic root, causing **aortic root dilation**, resulting in **aortic valve incompetence**.

THORACIC AORTIC DISSECTION	THORACIC AORTIC ANEURYSM	ABDOMINAL AORTIC ANEURYSM
Career hypertension and vasa vasorum hyaline arteriolosclerosis	Tertiary syphilis and compromised vasa vasorum lumen	Atherosclerosis compromising inner tunica media
Marfan's, Ehlers-Danlos, Loeys-Dietz		

Table 3.1: Licensing Exam Associations
The hard associations are for licensing examinations more than for clinical practice. Associate thoracic aneurysms with tertiary syphilis, called syphilitic aortitis.

Coarctation of the Aorta

The aorta exits the left ventricle on the right side of the heart, arches over the pulmonary artery, and then descends in the posterior mediastinum into the abdomen. In fetal development, the ductus arteriosus connects the pulmonary artery to the aorta distal to the branches that feed the head and arms. When the ductus arteriosus closes, it becomes the ligamentum arteriosum.

Coarctation of the aorta is stenosis, a narrowing of the aortic arch. There are two presentations: the infantile form with an open ductus and an adult form with a closed ductus.

Infantile form. The coarctation occurs proximal to the ductus arteriosus, and the **ductus arteriosus stays open**. The coarctation allows oxygenated blood to the brain but restricts delivery of blood distal to the coarctation. Because the ductus is open, the **deoxygenated blood from the right ventricle** is allowed to be distributed to the lower extremities. The blood mixes—some oxygenated blood from

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the aorta gets through—but there is still relatively deoxygenated blood in the lower extremities. This presents with **cyanosis** or **claudication when learning to walk**. This is usually found in the first year of life. Patients with the genetic disease **Turner syndrome** (45,XO) will present with a coarctation, often the infantile form.

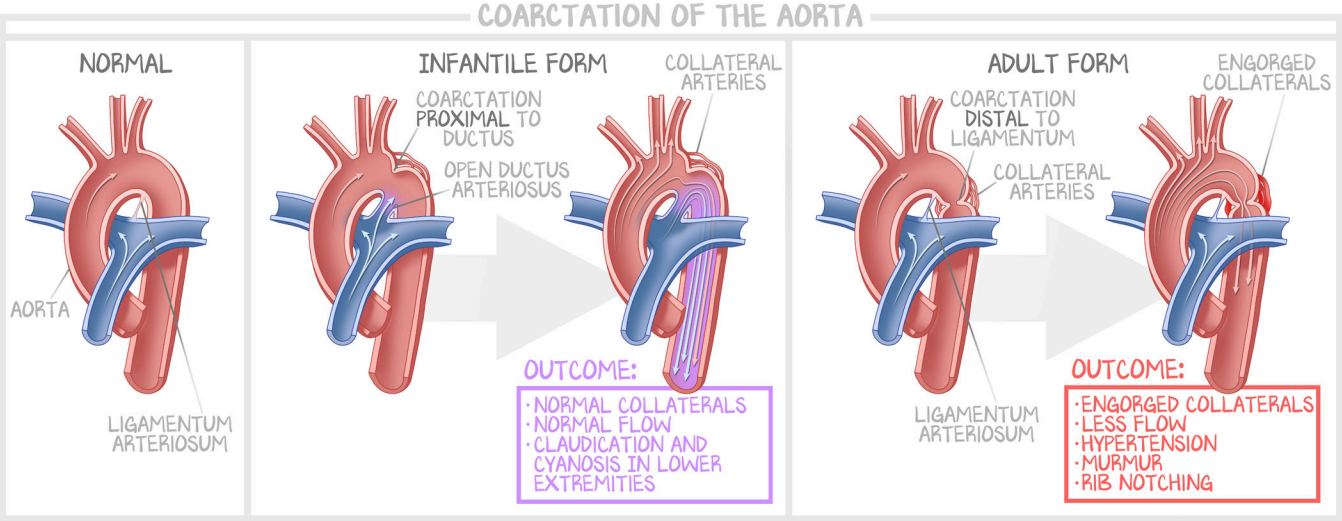

Figure 3.7: Coarctation of the Aorta
Normal development shows the aortic arch, the closed ductus arteriosus as the ligamentum arteriosum, and no stenosis. In the infantile form, the coarctation is proximal to the ductus arteriosus, and the ductus is open, sending deoxygenated blood to the lower extremities, provoking claudication (leg pain) when trying to walk. In the adult form, the coarctation is distal to the ductus arteriosus, which closes to the ligamentum arteriosum, presenting as excess perfusion to the upper extremities and decreased perfusion to the lower extremities.

The **adult** type can present at any time in life and is a coarctation **with a closed ductus arteriosus**. When the ductus closes, there is increased resistance in the delivery of blood to the lower extremities. This results in hypertension in the upper extremities with hypotension in the lower extremities. This mismatch is called a **brachial-femoral delay** (lots of pulses in the brachial artery, not a lot of pulses in the femoral artery). The area of flow in the aorta is reduced, creating turbulence. There may be a **murmur**, a systolic ejection murmur that can be heard in the interscapular region. With age, collateral circulation develops around the coarctation, resulting in thoracic artery engorgement, which subsequently erodes the ribs, resulting in **rib notching** on X-ray. Longstanding coarctations act as an increased vascular resistance, which can result in left concentric ventricular hypertrophy. Although coarctation can occur as a solitary defect, the adult form is associated (in about 50% of cases) with a bicuspid aortic valve.

If the coarctation is severe, the adult form (closed ductus) can present like the infantile form (open ductus).

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DIAGNOSIS	PATHOGENESIS	LOCATION	PRESENTATION
Aortic dissection	Hyaline arteriosclerosis (means "career HTN") Marfan's Ehlers-Danlos	Ascending aorta	Tearing chest pain radiating to the back Unequal blood pressures in the arms Widened mediastinum on X-ray Confirm with CT angiogram Retrograde progression results in pericardial tamponad
Thoracic aneurysm	Syphilis arteritis	Thoracic aorta	Compression of mediastinal structures (cough, dysphagia, hoarseness) Progression results in aortic insufficiency Low socioeconomic status with a history of STIs and risky sexual behaviors
Abdominal aneurysm	Atherosclerosis	Abdominal aorta	Asymptomatic pulsatile mass in the abdomen Or Severe back pain with a pulsating mass Men, smokers ≥ 65 years old Progression involves renal arteries or mural thrombus Screen with ultrasound, avoid angiogram, CTA is OK
Infantile Coarctation	Patent ductus arteriosus Turner syndrome	Proximal ductus	Claudication when learning to walk Cyanosis with exercise Right-heart hypertrophy
Adult Coarctation	Closed ductus Arteriosus Bicuspid aorta	Distal ductus, ductus closed	Brachial-femoral delay, HTN in arms, HypoTN in legs Systolic murmur heard in back Rib notching (collateral), left-heart hypertrophy

Table 3.2: Main Diseases of the Aorta
Because there is so much overlap in aneurysmal diseases, from mechanism to complication, we recommend separating them into three distinct diseases without any overlap. Because the severity of coarctation and patency of the ductus can mimic one another, we recommend you simplify by memorizing them as two distinct diseases.

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